

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 October 2004 (21.10.2004)

PCT

(10) International Publication Number  
**WO 2004/090551 A3**

(51) International Patent Classification<sup>7</sup>: **G01N 33/68**

(21) International Application Number:  
PCT/EP2004/003737

(22) International Filing Date: 7 April 2004 (07.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/461,558 8 April 2003 (08.04.2003) US  
60/461,623 8 April 2003 (08.04.2003) US  
60/471,479 16 May 2003 (16.05.2003) US  
60/474,863 30 May 2003 (30.05.2003) US  
60/484,140 30 June 2003 (30.06.2003) US

(71) Applicant (for all designated States except US): **GEN-OVA, LTD.**; Canon's Court, 22 Victoria Street, Hamilton, HM12 (BM).

(71) Applicant (for AT only): **NOVARTIS PHARMA GMBH** [AT/AT]; Brunner Strasse 59, I-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ARGOUD-PUY,**

**Guilaine** [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, 1217 Meyrin (CH). **BEDERR, Nassima** [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin (CH). **BOUGUELERET, Lydie** [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin (CH). **CUSIN, Isabelle** [FR/CH]; c/o GeneProt, Inc., 2, rue Pre-de-la-Fontaine, CH-1217 Meyrin (CH). **MAHE, Eve** [FR/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin (CH). **NIKNEJAD, Anne** [CH/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin (CH). **REFFAS, Samia** [CH/CH]; c/o GeneProt, Inc., 2, Pre-de-la-Fontaine, CH-1217 Meyrin (CH).

(74) Agent: **GRUBB, Philip**; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

[Continued on next page]

(54) Title: **SECRETED POLYPEPTIDE SPECIES ASSOCIATED WITH CARDIOVASCULAR DISORDERS**

**SEQ ID NO:1**

1 APGPRGIIIN LENGELCMNS AQCKSNCCQH SSALGLARCT SMASENSECS VKTLYGIYYK  
61 CPCERGLTCE GDKTIVGSIT NTNFGICHDA GRSKQ

**SEQ ID NO:2**

1 GIIINLENGE LCMNSAQCKS NCCQHSSALG LARCTSMASE NSECSVKTLY GIYYKPCER  
61 GLTCEGDKTI VGSITNTNFG ICHDAGRSKQ

**SEQ ID NO:3**

1 SNCCQHSSAL GLAR

**SEQ ID NO:4**

1 CTSMASENSE CSVK

**SEQ ID NO:5**

1 TIVGSITNTN FGICHDAGR

(57) Abstract: The invention discloses human secreted polypeptides that circulate at an increased level in the plasma of patients with cardiovascular disorders. The invention also provides methods of using compositions including the polypeptides, polynucleotides encoding them, and antibodies specific for these polypeptides, for diagnosis, prognosis, and for drug development.

WO 2004/090551 A3



PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) **Date of publication of the international search report:**

20 January 2005

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/003737

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHAPUS C ET AL: "ROLE OF COLIPASE IN THE INTERFACIAL ADSORPTION OF PANCREATIC LIPASE AT HYDROPHILIC INTERFACES" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 58, no. 1, 1 October 1975 (1975-10-01), pages 155-158, XP002041838 ISSN: 0014-5793 the whole document</p> <p style="text-align: center;">----- -/--</p>	1-16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*B\* document member of the same patent family

Date of the actual completion of the international search

16 August 2004

Date of mailing of the international search report

29. 11. 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Weijland, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/003737

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MAHE-GOUHIER N ET AL: "IMMOBILIZED COLIPASE AFFINITIES FOR LIPASES B, A, C AND THEIR TERMINAL PEPTIDE (336-449): THE LIPASE RECOGNITION SITE LYSINE RESIDUES ARE LOCATED IN THE C-TERMINAL REGION" BBA - LIPIDS AND LIPID METABOLISM, ELSEVIER SCIENCE BV. AMSTERDAM, NL, vol. 962, 1988, pages 91-97, XP002041839 ISSN: 0005-2760 the whole document	1-16
A	WO 03/023397 A (LIU KAN-ZHI ; MANTSCH HENRY H (CA); NAT RES COUNCIL (CA); SHAW ANTHONY) 20 March 2003 (2003-03-20) the whole document	1-16
A	US 6 503 540 B1 (BADER DAVID M ET AL) 7 January 2003 (2003-01-07) the whole document	1-16
X	WO 98/30588 A (CHAPUS CATHERINE ; LAPHAL LABORATOIRE DE PHARMACO (FR)) 16 July 1998 (1998-07-16) abstract page 3, paragraph 6	8,13
A	WO 02/06840 A (BIOPREVENTIVE LTD ; GALILI NACHSHON NITSA (IL); RUBIN YORAM (IL); NIMR) 24 January 2002 (2002-01-24) the whole document	1-16
X	WO 98/17807 A (BIOCEM S A ; MEROT BERTRAND (FR); BOURNAT PHILIPPE (FR); GRUBER VERONI) 30 April 1998 (1998-04-30) page 25, line 1 - line 17	9,10

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/003737

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03023397	A	20-03-2003	CA 2357338 A1	12-03-2003
			WO 03023397 A1	20-03-2003
			CA 2459349 A1	20-03-2003
			EP 1428022 A1	16-06-2004
US 6503540	B1	07-01-2003	NONE	
WO 9830588	A	16-07-1998	FR 2758143 A1	10-07-1998
			AT 273995 T	15-09-2004
			AU 727469 B2	14-12-2000
			AU 5868698 A	03-08-1998
			BR 9806857 A	14-03-2000
			CA 2277778 A1	16-07-1998
			CN 1248264 T	22-03-2000
			CZ 9902414 A3	12-01-2000
			DE 69825733 D1	23-09-2004
			EP 0970118 A1	12-01-2000
			WO 9830588 A1	16-07-1998
			HU 0001458 A2	28-10-2000
			NZ 337087 A	26-01-2001
			US 6432400 B1	13-08-2002
			ZA 9800094 A	08-07-1998
WO 0206840	A	24-01-2002	AU 7272801 A	30-01-2002
			CA 2414897 A1	24-01-2002
			EP 1299731 A2	09-04-2003
			WO 0206840 A2	24-01-2002
			US 2004015101 A1	22-01-2004
WO 9817807	A	30-04-1998	FR 2754827 A1	24-04-1998
			AU 4871997 A	15-05-1998
			CA 2269025 A1	30-04-1998
			EP 0941343 A1	15-09-1999
			WO 9817807 A1	30-04-1998
			JP 2001507928 T	19-06-2001

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/003737

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 14-16 (with respect to industrial applicability)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 14-16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-16 (part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-16 (partially)

1. Claims 1-16 (partially)

Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of a treatment etc. using SEQ ID NOs 1-5 involving colipase

---

2. claims: 1-16 (partially)

2. Claims 1-16 (partially)

Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOs 6-10 involving eosinophil-derived neurotoxin

---

3. claims: 1-16 (partially)

Claims 1-16 (partially)

Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc using SEQ ID Nos 11-14 involving human epididymal secretory protein.

---

4. claims: 1-16 (partially)

Claims 1-16 (partially)

Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOS 15-23 involving Defensin I

---

5. claims: 1-16 (partially)

Claims 1-16 (partially)

Screening methods and/or diagnosis, prediction, identifying modulators, monitoring the efficacy of treatment etc. using SEQ ID NOs 24-28 involving plasminogen-related protein B

---